view of Bennett et al. (US Patent 5,955,443). The Examiner suggests that it would have been *prima facie* obvious to one of ordinary skill make and use antisense oligonucleotides targeting the 5'-untranslated region, the start codon region, the stop codon region, or the 3'-untranslated region of human cholesteryl ester transfer protein. The Examiner suggests it would have been obvious to incorporate the modifications as taught by Bennett et al. into the antisense of Liu et al. or antisense designed from the complementary sequence of Drayna et al., because Bennett teach the desirability of such modifications. The Examiner suggests one of skill would have been motivated to create such compounds due to the teaching of Liu et al. and Drayna et al. regarding the significance of this protein in disease. The Examiner suggests one of skill would have had an expectation of success based on the teachings of Liu et al. and Bennett et al. Applicants respectfully traverse this rejection.

At the outset, claim 1 and its dependent claims have been amended as discussed *supra* to recite antisense compounds targeted to specific nucleobase regions within the 5'-untranslated region, the start codon region, the stop codon region, or the 3'-untranslated region of human cholesteryl ester transfer protein of

SEQ ID NO: 3. Support for these amendments can be found at pages 99-100 of the specification as filed.

Liu et al. (1999) disclose only a single antisense compound that is targeted to a specific area of the nucleic acid sequence of Drayna et al. Nowhere does this reference teach or suggest antisense compounds targeted to human cholesteryl ester transfer protein as claimed, including specific regions of human cholesteryl ester transfer protein of SEQ ID NO: 3. Therefore, this primary reference fails to teach the limitations of the claims.

Drayna et al. (1987) discloses the sequence of human cholesteryl ester transfer protein. Nowhere does this reference teach or suggest antisense compounds of any type targeted to human cholesteryl ester transfer protein as now claimed, including specific regions of human cholesteryl ester transfer protein. Therefore, this primary reference also fails to teach the limitations of the claims.

The secondary reference cited fails to overcome the deficiencies in teaching of the primary references.

Bennett et al. (US Patent 5,955,443) teaches methods of modifying antisense oligonucleotides to enhance activity. However, nowhere does this patent teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to human

cholesteryl ester transfer protein nucleic acid molecules, or any region of a human cholesteryl ester transfer protein nucleic acid molecule.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific nucleobase regions of a nucleic acid molecule encoding human cholesteryl ester transfer protein, and thus cannot render the instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: **February 20, 2003**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been amended as follows:

1. (trice amended) A compound 8 to 50 nucleobases in length targeted to nucleobases 31 through 110 of a 5'-untranslated region, nucleobases 121 through 150 of a start codon region, ~~nucleobases 161 through 170, nucleobases 201 through 220, nucleobases 311 through 320, nucleobases 351 through 370, nucleobases 446 through 465, nucleobases 641 through 660, nucleobases 711 through 730, nucleobases 771 through 790, nucleobases 799 through 818, nucleobases 1041 through 1060, nucleobases 1061 through 1080, nucleobases 1411 through 1430, or nucleobases 1571 through 1590 of a coding region,~~ nucleobases 1600 through 1620 of a stop codon region, or nucleobases 1631 through 1769 of a 3'-untranslated region of a nucleic acid molecule encoding cholesteryl ester transfer protein (SEQ ID NO: 3), wherein said compound specifically hybridizes with one of said regions and inhibits the expression of cholesteryl ester transfer protein.